



SEQUENCE LISTING

<110> Protein Design Labs, Inc.
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<120> Chimeric and Humanized Antibodies to alpha5beta1 Integrin That Modulate Angiogenesis

<130> 05882.0178.NPUS01

<140> 10/724,274
<141> 2003-11-26

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<151> 2002-11-26

<150> 60/508,149
<151> 2003-09-30

<160> 47

<170> PatentIn version 3.2

<210> 1
<211> 124
<212> PRT
<213> mus musculus

<400> 1

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
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Ser Leu Ser Ile Thr Cys Thr Ile Ser Gly Phe Ser Leu Thr Asp Tyr
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Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr Tyr Cys Ala
85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

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<212> PRT
<213> Artificial Sequence Sequence

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Gln Val Gln Leu Val Glu Ser Gly Pro Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Ile Ser Cys Ala Ile Ser Gly Phe Ser Leu Thr Asp Tyr
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Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Met Thr Ile Ser Lys Asp Asn Ser Lys Ser Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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<212> PRT
<213> Artificial Sequence Sequence

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<400> 3

Glu Val Gln Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Ile Ser Cys Ala Ile Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Met Thr Ile Ser Lys Asp Asn Ser Lys Asn Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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<212> PRT
<213> Artificial Sequence

<220>
<223> humanized antibody

<400> 4

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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<212> PRT
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<223> humanized antibody

<400> 5

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Ser Leu Arg Leu Ser Cys Ala Ile Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Met Thr Ile Ser Lys Asp Asn Ser Lys Ser Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Ile Ser Cys Ala Ile Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Met Thr Ile Ser Lys Asp Asn Ser Lys Ser Thr Val Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys Ala
85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 7
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<212> PRT
<213> mus musculus

<400> 7

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
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Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Asn
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ala Pro Asn Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro
85 90 95

Pro Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys Arg
100 105

<210> 8
<211> 109
<212> PRT
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<220>
<223> humanized antibody

<400> 8

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Met Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Asn
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Met Gln
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro
85 90 95

Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
100 105

<210> 9
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<212> PRT
<213> Artificial Sequence

<220>
<223> humanized antibody

<400> 9

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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Asp Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Asn
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Met Gln
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro
85 90 95

Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg
Page 6

100

105

<210> 10
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<223> humanized antibody

<400> 10

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Asn
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro
85 90 95

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 11
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<223> humanized antibody

<400> 11

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Asn
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
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50

55

60

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro
85 90 95

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 12

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<212> PRT

<213> Artificial Sequence

<220>

<223> humanized antibody

<400> 12

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Asn
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln
65 70 75 80

Pro Glu Asp Phe Ala Thr Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro
85 90 95

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

<210> 13

<211> 429

<212> DNA

<213> mus musculus

<400> 13

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tgcaccatct cagggttctc attaaccgac tatgggttcc actgggttcg ccagcctcca 180

gaaaagggtc tggagtggct ggtagtgatt tggagtgatg gaagctcaac ctataattca 240
gctctcaa at ccagaatgac catcaggaag gacaactcca agagccaagt tttcttaata 300
atgaacagtc tccaaactga tgactcagcc atgtactact gtgccagaca tggaacttac 360
tacggtatga ctacgacggg ggatgcttt gactactggg gtcaaggaac ctcagtcacc 420
gtctcctca 429

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<212> DNA
<213> mus musculus

<400> 14
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agaggacaaa ttgttctcac ccagtctcca gcaatcatgt ctgc atctctc agggAACGG 120
gtcaccatga cctgcactgc cagttcaagt gtaagttcca attacttgca ctggtaccag 180
cagaagccag gatccgcccc caatctctgg atttata tagca catccaacct ggcttctgga 240
gtcccagctc gttcagttgg cagtgggtct gggacctctt actctctcac aatcagcagc 300
atggaggctg aagatgctgc cacttattac tgccaccagt atcttcgttc cccaccgacg 360
ttcggtgag gcaccaagct gaaaaatcaaa 390

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<211> 429
<212> DNA
<213> Artificial Sequence

<220>
<223> chimeric antibody

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tgcaccatct cagggttctc attaaccgac tatggtgttc actgggttcg ccagcctcca 180
gaaaagggtc tggagtggct ggtagtgatt tggagtgatg gaagctcaac ctataattca 240
gctctcaa at ccagaatgac catcaggaag gacaactcca agagccaagt tttcttaata 300
atgaacagtc tccaaactga tgactcagcc atgtactact gtgccagaca tggaacttac 360
tacggtatga ctacgacggg ggatgcttt gactactggg gtcaaggaac ctcagtcacc 420
gtctcgagc 429

<210> 16
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<213> Artificial Sequence

<220>

<223> chimeric antibody

<400> 16

Met Ala Val Leu Gly Leu Leu Leu Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala
20 25 30

Pro Ser Gln Ser Leu Ser Ile Thr Cys Thr Ile Ser Gly Phe Ser Leu
35 40 45

Thr Asp Tyr Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu
50 55 60

Glu Trp Leu Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser
65 70 75 80

Ala Leu Lys Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln
85 90 95

Val Phe Leu Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr
100 105 110

Tyr Cys Ala Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp
115 120 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
130 135 140

<210> 17

<211> 390

<212> DNA

<213> Artificial Sequence

<220>

<223> chimeric antibody

<400> 17

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gtcaccatga cctgcactgc cagttcaagt gtaagttcca attacttgca ctggtaccag 180

cagaagccag gatccGCCC caatctctgg atttatagca catccaacct ggcttctgga 240

gtcccagctc gttcagtg ggtaggggtct gggacctctt actctctcac aatcagcagc 300

atggaggctg aagatgctgc cacttattac tgccaccagt atcttcgttc cccaccgacg 360

ttcgggtggag gcaccaagct cgagatcaa 390

<210> 18
<211> 130
<212> PRT
<213> Artificial Sequence

<220>
<223> chimeric antibody

<400> 18

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Gly Gln Ile Val Leu Thr Gln Ser Pro Ala Ile
20 25 30

Met Ser Ala Ser Leu Gly Glu Arg Val Thr Met Thr Cys Thr Ala Ser
35 40 45

Ser Ser Val Ser Ser Asn Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly
50 55 60

Ser Ala Pro Asn Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly
65 70 75 80

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
85 90 95

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His
100 105 110

Gln Tyr Leu Arg Ser Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu
115 120 125

Ile Lys
130

<210> 19
<211> 459
<212> DNA
<213> Artificial Sequence

<220>
<223> chimeric antibody

<400> 19
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tgtccatcac atgcaccatc tcagggttct cattaaccga ctatggtgtt cactgggttc 180
gccagcctcc aggaaagggt ctggagtgcc tggtagtgat ttggagtgtat ggaagctcaa 240

cctataattc agctctcaa tccagaatga ccatcaggaa ggacaactcc aagagccaag 300
tttcttaat aatgaacagt ctccaaactg atgactcagc catgtactac tgtgccagac 360
atggaactta ctacggaatg actacgacgg gggatgctt ggactactgg ggtcaaggaa 420
cctcagtcac cgtctcctca ggtaagaatg gcctctaga 459

<210> 20
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<212> PRT
<213> Artificial Sequence

<220>
<223> chimeric antibody

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Met Ala Val Leu Gly Leu Leu Leu Cys Leu Val Thr Phe Pro Ser Cys
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Val Leu Ser Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala
20 25 30

Pro Ser Gln Ser Leu Ser Ile Thr Cys Thr Ile Ser Gly Phe Ser Leu
35 40 45

Thr Asp Tyr Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu
50 55 60

Glu Trp Leu Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser
65 70 75 80

Ala Leu Lys Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln
85 90 95

Val Phe Leu Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr
100 105 110

Tyr Cys Ala Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp
115 120 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
130 135 140

<210> 21
<211> 425
<212> DNA
<213> Artificial Sequence

<220>
<223> chimeric antibody

<400> 21

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taggggaacg ggtcaccatg acctgcactg ccagttcaag tgtcagttcc aattacttgc 180
actggtacca gcagaagcca ggatccgccc ccaatctctg gatttatagc acatccaacc 240
tggcttctgg agtcccagct cgttcagtg gcagtggtc tggacacctct tactctctca 300
caatcagcag catggaggct gaagatgctg ccacttatta ctgccaccag tatcttcgtt 360
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ctaga 425

<210> 22
<211> 130
<212> PRT
<213> Artificial Sequence

<220>
<223> chimeric antibody
<400> 22

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Gly Gln Ile Val Leu Thr Gln Ser Pro Ala Ile
20 25 30

Met Ser Ala Ser Leu Gly Glu Arg Val Thr Met Thr Cys Thr Ala Ser
35 40 45

Ser Ser Val Ser Ser Asn Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly
50 55 60

Ser Ala Pro Asn Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly
65 70 75 80

Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu
85 90 95

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His
100 105 110

Gln Tyr Leu Arg Ser Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu
115 120 125

Ile Lys
130

<210> 23

<211> 1353
<212> DNA
<213> Artificial Sequence

<220>
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<400> 23
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ccaggaaagg gtctggagtg gctggtagtg atttggagtg atggaagctc aacctataat 180
tcagctctca aatccagaat gaccatcagg aaggacaact ccaagagcca agtttctta 240
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tactacggaa tgactacgac gggggatgct ttggactact ggggtcaagg aacctcagtc 360
accgtctcct cagcttccac caagggccca tccgtcttcc ccctggcgcc ctgctccagg 420
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aacagcacgt accgtgtggt cagcgtccctc accgtcctgc accaggactg gctgaacggc 960
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gtgctggact ccgacggctc cttcttcctc tacagcaggc taaccgtgga caagagcagg 1260
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acacagaaga gcctctccct gtctctgggt aaa 1353

<210> 24
<211> 645
<212> DNA
<213> Artificial Sequence

<220>
<223> chimeric antibody

<400> 24

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ccaggatccg cccccaatct ctggatttat agcacatcca acctggcttc tggagtccc 180
gctcgttca gtggcagtgg gtctgggacc tcttactctc tcacaatcatcag cagcatggag 240
gctgaagatg ctgccactta ttactgccac cagtatcttc gttccccacc gacgttcggt 300
ggaggcacca agctggaaat caaacgaact gtggctgcac catctgtctt catcttccc 360
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tatcccagag aggccaaagt acagtggaaag gtggataacg ccctccaatc gggtaactcc 480
caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg 540
acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag 600
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<210> 25
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> chimeric antibody

<400> 25

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

Ser Leu Ser Ile Thr Cys Thr Ile Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr Tyr Cys Ala
85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
130 135 140

Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145 150 155 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
165 170 175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
180 185 190

Val Thr Val Pro Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn
195 200 205

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser
210 215 220

Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln
260 265 270

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Leu Gly Lys
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<210> 26
<211> 215
<212> PRT
<213> Artificial Sequence

<220>
<223> chimeric antibody

<400> 26

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Leu Gly
1 5 10 15

Glu Arg Val Thr Met Thr Cys Thr Ala Ser Ser Ser Val Ser Ser Asn
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Ser Ala Pro Asn Leu Trp
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu
65 70 75 80

Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro
85 90 95

Pro Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
Page 17

| | | |
|---|-----|-----|
| 130 | 135 | 140 |
| Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser | | |
| 145 | 150 | 155 |
| Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu | | |
| 165 | 170 | 175 |
| Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val | | |
| 180 | 185 | 190 |
| Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys | | |
| 195 | 200 | 205 |
| Ser Phe Asn Arg Gly Glu Cys | | |
| 210 | 215 | |

<210> 27
<211> 696
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ccagggaaagg gtctggagtg gctggtagtg atttggagtg atggaagctc aacctataat 120
tcagctctca aatccagaat gaccatcagg aaggacaact ccaagagcca agttttctta
ataatgaaca gtctccaaac tgatgactca gccatgtact actgtgccag acatggaact
tactacggaa tgactacgac gggggatgct ttggactact ggggtcaagg aacctcagtc 300
accgtctcct cagcttccac caagggccca tccgtttcc ccctggcgcc ctgctccagg
agcacctccg agagcacagc cgccctggc tgcctggta aggactactt cccgaaccg 420
gtgacggtgt cgtggaactc aggcgcctg accagcggcg tgcacacctt cccggctgtc
ctacagtccct caggactcta ctccctcagc agcgtggta ccgtgccctc cagcagctg 540
ggcacgaaga cctacacctg caacgtagat cacaagccca gcaacaccaa ggtggacaag
agagttgagt ccaaatatgg tcccccatgc ccatca 660
696

<210> 28
<211> 232
<212> PRT
<213> Artificial Sequence
<220>
<223> chimeric antibody

<400> 28

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
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Ser Leu Ser Ile Thr Cys Thr Ile Ser Gly Phe Ser Leu Thr Asp Tyr
20 25 30

Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr Tyr Cys Ala
85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
100 105 110

Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys
115 120 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
130 135 140

Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145 150 155 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
165 170 175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
180 185 190

Val Thr Val Pro Ser Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn
195 200 205

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser
210 215 220

Lys Tyr Gly Pro Pro Cys Pro Ser
225 230

<210> 29

<211> 1353
 <212> DNA
 <213> Artificial Sequence

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 <400> 29
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 ccaggaaagg gtctggagtg gctgggttg atttggagtg atggaagctc aacctataat 180
 tcagctctca aatccagaat gaccatctca aaggacaacg ccaagaacac cgttactta 240
 cagatgaaca gtctcagac tgaggacacc gccgtgtact actgtgccag acatggaact 300
 tactacggaa tgactacgac gggggatgct ttggactact ggggtcaagg aaccctggtc 360
 accgtctcct cagttccac caagggccca tccgtttcc ccctggcgcc ctgctccagg 420
 agcacctccg agagcacacgc cgccctggc tgcctggta aggactactt ccccgAACCG 480
 gtgacggtgt cgtggaaactc aggcccccctg accagccgcg tgcacacctt cccggctgtc 540
 ctacagtccct caggactcta ctccctcagc agcgtggta ccgtcccccc cagcagctt 600
 ggcacgaaga cctacacctg caacgttagat cacaagccca gcaacaccaa ggtggacaag 660
 agagttgagt ccaaatatgg tcccccatgc ccatcatgcc cagcacctga gttcctgggg 720
 ggaccatcag tttccctgtt ccccccaaaa cccaaggaca ctctcatgat ctccggacc 780
 cctgaggtca cgtgcgttgt ggtggacgtg agccaggaag accccgaggt ccagttcaac 840
 tggtacgtgg atggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagttc 900
 aacagcacgt accgtgttgt cagcgtccctc accgtcctgc accaggactg gctgaacggc 960
 aaggagtaca agtgcaaggt ctccaacaaa ggcctccgt cctccatcga gaaaaccatc 1020
 tccaaagcca aaggccagcc ccgagagcca caggtgtaca ccctgcccccc atcccaggag 1080
 gagatgacca agaaccaggt cagcctgacc tgcctggta aaggcttcta ccccaAGCAG 1140
 atcgccgtgg agtggagag caatggcag ccggagaaca actacaagac cacgcctccc 1200
 gtgctggact ccgacggctc cttcttcctc tacagcaggc taaccgtgga caagagcagg 1260
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 acacagaaga gcctccct gtctctgggt aaa 1353

<210> 30
 <211> 645
 <212> DNA
 <213> Artificial Sequence

 <220>
 <223> chimeric antibody

 <400> 30

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| ctctcctgca ctgccagtgc aagtgtcagt tccaattact tgcactggta ccagcagaag | 120 |
| ccaggacagg ccccccgtct cctcatttat agcacatcca acctggcttc tggagtccca | 180 |
| gctcgttca gtggcagtgg gtctgggacc tcttacaccc tcacaatcag cagcctcgag | 240 |
| ccagaagatt tcgccgtcta ttactgccac cagtatcttc gttccccacc gacgttcggt | 300 |
| ggagggacca aggtcgaaat caaacgaact gtggctgcac catctgtctt catcttcccg | 360 |
| ccatctgatg agcagttgaa atctggaact gcctctgttg tgtgcctgct gaataacttc | 420 |
| tatcccagag aggccaaagt acagtggaaag gtggataacg ccctccaatc gggtaactcc | 480 |
| caggagagtg tcacagagca ggacagcaag gacagcacct acagcctcag cagcaccctg | 540 |
| acgctgagca aagcagacta cgagaaacac aaagtctacg cctgcgaagt caccatcag | 600 |
| ggcctgagct cgcccggtcac aaagagcttc aacaggggag agtgt | 645 |

<210> 31
 <211> 451
 <212> PRT
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<220>
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 <400> 31

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asp Tyr
 20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Leu
 35 40 45

Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser Ala Leu Lys
 50 55 60

Ser Arg Met Thr Ile Ser Lys Asp Asn Ala Lys Asn Thr Val Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
 85 90 95

Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp Ala Leu Asp
 100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys
 115 120 125

Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu
130 135 140

Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro
145 150 155 160

Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr
165 170 175

Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val
180 185 190

Val Thr Val Pro Ser Ser Leu Gly Thr Lys Thr Tyr Thr Cys Asn
195 200 205

Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Ser
210 215 220

Lys Tyr Gly Pro Pro Cys Pro Ser Cys Pro Ala Pro Glu Phe Leu Gly
225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser Gln
260 265 270

Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr
290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser Ser Ile
325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
340 345 350

Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln Val Ser
355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu Thr Val
405 410 415

Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser Val Met
420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
435 440 445

Leu Gly Lys
450

<210> 32
<211> 215
<212> PRT
<213> Artificial Sequence

<220>
<223> chimeric antibody

<400> 32

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Thr Ala Ser Ser Ser Val Ser Ser Asn
20 25 30

Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Ser Tyr Thr Leu Thr Ile Ser Ser Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys His Gln Tyr Leu Arg Ser Pro
85 90 95

Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
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| | | |
|---|-----|-----|
| 130 | 135 | 140 |
| Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser | | |
| 145 | 150 | 155 |
| Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu | | |
| 165 | 170 | 175 |
| Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val | | |
| 180 | 185 | 190 |
| Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys | | |
| 195 | 200 | 205 |
| Ser Phe Asn Arg Gly Glu Cys | | |
| 210 | 215 | |
| <210> 33 | | |
| <211> 6 | | |
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| <220> | | |
| <223> oligonucleotide | | |
| <400> 33 | | |
| ctcgag | | |
| 6 | | |
| <210> 34 | | |
| <211> 6 | | |
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| <213> Artificial Sequence | | |
| <220> | | |
| <223> oligonucleotide | | |
| <400> 34 | | |
| tctaga | | |
| 6 | | |
| <210> 35 | | |
| <211> 6 | | |
| <212> DNA | | |
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| <223> oligonucleotide | | |
| <400> 35 | | |
| acgcgt | | |
| 6 | | |
| <210> 36 | | |
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| <212> DNA | | |
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| <220> | | |
| <223> | oligonucleotide | |
| <400> | 36 | |
| | ttttctagac caccatggct gtcctggggc tgctt | 35 |
| <210> | 37 | |
| <211> | 47 | |
| <212> | DNA | |
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| <220> | | |
| <223> | oligonucleotide | |
| <400> | 37 | |
| | ttttctagag gttgtgagga ctcacctgag gagacggta ctgaggt | 47 |
| <210> | 38 | |
| <211> | 31 | |
| <212> | DNA | |
| <213> | Artificial Sequence | |
| <220> | | |
| <223> | oligonucleotide | |
| <400> | 38 | |
| | tggaaacctac tacggaatga ctacgacggg g | 31 |
| <210> | 39 | |
| <211> | 31 | |
| <212> | DNA | |
| <213> | Artificial Sequence | |
| <220> | | |
| <223> | oligonucleotide | |
| <400> | 39 | |
| | ccccgtcgta gtcattccgt agtaagttcc a | 31 |
| <210> | 40 | |
| <211> | 43 | |
| <212> | DNA | |
| <213> | Artificial Sequence | |
| <220> | | |
| <223> | oligonucleotide | |
| <400> | 40 | |
| | ttttctagag gccattctta cctgaggaga cggtgactga ggt | 43 |
| <210> | 41 | |
| <211> | 35 | |
| <212> | DNA | |
| <213> | Artificial Sequence | |
| <220> | | |
| <223> | oligonucleotide | |
| <400> | 41 | |

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|---|----|
| tttacgcgtc caccatggat tttcaggtgc agatt | 35 |
| <210> 42 | |
| <211> 49 | |
| <212> DNA | |
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| <220> | |
| <223> oligonucleotide | |
| <400> 42 | |
| ttttcttagat taggaaagtg cacttacgtt tgattccag cttggtgcc | 49 |
| <210> 43 | |
| <211> 31 | |
| <212> DNA | |
| <213> Artificial Sequence | |
| <220> | |
| <223> oligonucleotide | |
| <400> 43 | |
| tgcaggatca agtgtcagtt ccaattactt g | 31 |
| <210> 44 | |
| <211> 31 | |
| <212> DNA | |
| <213> Artificial Sequence | |
| <220> | |
| <223> oligonucleotide | |
| <400> 44 | |
| caagtaattg gaactgacac ttgaactggc a | 31 |
| <210> 45 | |
| <211> 48 | |
| <212> DNA | |
| <213> Artificial Sequence | |
| <220> | |
| <223> oligonucleotide | |
| <400> 45 | |
| ttttcttagac tttggattct acttacgtt gattccagc ttggtgcc | 48 |
| <210> 46 | |
| <211> 143 | |
| <212> PRT | |
| <213> mus musculus | |
| <400> 46 | |
| Met Ala Val Leu Gly Leu Leu Leu Cys Leu Val Thr Phe Pro Ser Cys | |
| 1 5 10 15 | |
| Val Leu Ser Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala | |
| 20 25 30 | |

Pro Ser Gln Ser Leu Ser Ile Thr Cys Thr Ile Ser Gly Phe Ser Leu
35 40 45

Thr Asp Tyr Gly Val His Trp Val Arg Gln Pro Pro Gly Lys Gly Leu
50 55 60

Glu Trp Leu Val Val Ile Trp Ser Asp Gly Ser Ser Thr Tyr Asn Ser
65 70 75 80

Ala Leu Lys Ser Arg Met Thr Ile Arg Lys Asp Asn Ser Lys Ser Gln
85 90 95

Val Phe Leu Ile Met Asn Ser Leu Gln Thr Asp Asp Ser Ala Met Tyr
100 105 110

Tyr Cys Ala Arg His Gly Thr Tyr Tyr Gly Met Thr Thr Thr Gly Asp
115 120 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser
130 135 140

<210> 47

<211> 130

<212> PRT

<213> mus musculus

<400> 47

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Gly Gln Ile Val Leu Thr Gln Ser Pro Ala Ile
20 25 30

Met Ser Ala Ser Leu Gly Glu Arg Val Thr Met Thr Cys Thr Ala Ser
35 40 45

Ser Ser Val Ser Ser Asn Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly
50 55 60

Ser Ala Pro Asn Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly
65 70 75 80

Val Pro Ala Arg Phe Ser Gly Ser Gly Thr Ser Tyr Ser Leu
85 90 95

Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys His
100 105 110

Gln Tyr Leu Arg Ser Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu
115 120 125

Ile Lys
130